

Remarks

Claims 43-54 and 63-82 are pending in the subject application. By this Amendment, Applicants have canceled claims 44, 46-54, 62, 64, 67, 70, and 73 and amended claims 43, 45, 63, 65, 66, 68, 69, 71, 72, and 75-80. Support for the amendments can be found throughout the subject specification and in the claims as originally filed. Entry and consideration of the amendments presented herein is respectfully requested. Accordingly, claims 43, 45, 63, 65, 66, 68, 69, 71, 72, and 74-82 are currently before the Examiner. Favorable consideration of the pending claims is respectfully requested.

As an initial matter, Applicants' representative contacted the Examiner to discuss the references (which are printouts of accession numbers of sequences from different databases) which are not indicated as considered. During a telephonic conference with the Examiner, she confirmed that the references had been considered and made of record and that the "arrow" on the Information Disclosure Statement was intended to be a continuation of her initials in the "Examiner Initials" column. For the Examiner's convenience, Applicants have provided a clean copy of Form PTO/SB/08 containing only the accession numbers and dates for citation numbers R39-R45 and respectfully request that the Examiner initial and return the form. It is also respectfully submitted that no fees are required for the consideration of the references identified as R39-R45 as they were timely provided to the Patent Office as required by 37 C.F.R. 1.98.

Claims 43-45 and 63-82 are rejected under 35 U.S.C. § 112, second paragraph, as indefinite. Applicants respectfully assert that the claims as filed are definite. The Office Action has rejected the claims on the basis that the claims are indefinite in omitting essential elements and for various antecedent basis issues. Applicants have amended the claims and respectfully submit that the amendments have corrected the issues noted in the Office Action. Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, second paragraph, is respectfully requested.

Claims 43-54 and 63-82 are rejected under 35 U.S.C. § 101 as lacking a specific asserted utility or a well established utility. Claims 43-45 and 63-82 are rejected under 35 U.S.C. § 112, first paragraph, as failing to teach how to use the claimed invention in view of the alleged lack of patentable utility. Specifically, the Office Action argues that claims are drawn to a method of screening compounds that modulate the activity of protein phosphatase 2A (PP2A) by testing the

activity of PP2A in the presence of a candidate compound. The Office Action further argues that the claimed invention lacks patentable utility as the specification fails to disclose or teach any biological significance to the activity of PP2A/B γ or the interaction between PP2A/B γ and KCNQ2. While the Office Action acknowledges that the specification asserts that the claimed polypeptides are associated with mental disorders, it is argued that the lack of support/evidence in the specification or record requires a finding that the claimed invention lacks patentable utility. Applicants traverse.

It appears that the Office Action has based the rejections of record on the presence or absence of data within the as-filed specification. Specifically, the Office Action argues “However, the evidence of record fails to support this assertion. The instant specification fails to present any evidence or sound scientific reasoning that the PP2A/B γ and KCNQ interaction has any significance with respect to any pathological condition, including mental disorders” (Office Action at page 4, last paragraph). Applicants respectfully submit that the articulated rationale for issuing these rejections is improper. As stated in the M.P.E.P and in case law, asserted utilities of an invention carry a presumption of enablement and/or utility and the **Patent Office** must make a *prima facie* showing that the claimed invention lacks utility and is not enabled in establishing a rejection under 35 U.S.C. §§101 and 112, first paragraph. The Patent Office must also articulate the factual assumptions and provide evidentiary support relied upon in establishing the *prima facie* showing. *See In re Gaubert*, 524 F.2d 1222, 1224, 187 U.S.P.Q. 664, 666 (C.C.P.A. 1975) (Accordingly, the PTO must do more than merely question operability - it must set forth factual reasons which would lead one skilled in the art to question the objective truth of the statement of operability). Applicants submit that the Office Action has failed to meet this burden and submit that a *prima facie* showing that the claimed invention lacks patentable utility has not been made in this matter. Thus, reconsideration and withdrawal of the rejections is respectfully requested.

However, assuming *arguendo*, that such a case has been made, Applicants respectfully submit that the Office Action has considered the utility issue is too narrow a context with respect to the presently claimed invention (*i.e.*, a method directed to screening of candidate modulators of PP2A). As disclosed in the as-filed specification, KCNQ2 (the polypeptide with which PP2A/B γ interacts) forms a functional potassium channel (see Example 9), is phosphorylated by kinases (see Example 7) and binds to PP2A/B γ (see Examples 3 and 6). Further, the as-filed specification clearly

shows that PP2A phosphatase is responsible for dephosphorylation of KCNQ2 (see Example 7, section 2.2) and the art generally recognized that the phosphorylation/dephosphorylation state of KCNQ channels was believed to be involved in the control of neuronal excitability (see specification, page 3, first full paragraph).

The art also recognized that kinases and phosphatases were involved in the modulation of KCNQ channels and that currents generated by such channels could be increased by kinases (specification at page 3, first full paragraph). Furthermore, as noted in Borsotto *et al.* (*Pharmacogenomics J.*, 2007, 7:123-132, a copy of which is attached hereto) and the as-filed specification (page 2, paragraph 1), the PP2A/B γ polypeptide is known to be brain and neuron specific and acts to target specific substrates to the PP2A core enzyme (see Borsotto *et al.*, page 124, first full paragraph, citing to a reference disclosing such an activity and published in 1998 [prior to the effective filing date of this application]; see also the as-filed specification at page 2, paragraph 1). Thus, it is respectfully submitted that methods of identifying compounds that modulate the binding of KCNQ2 and PP2A/B γ or a PP2A phosphatase containing this subunit (and the compounds themselves) have utility as potential therapeutic agents for the treatment of mental disorders, such as bipolar disorder (particularly in view of the experimental data in the specification demonstrating that KCNQ2 (the polypeptide with which PP2A/B γ interacts) forms a functional potassium channel (see Example 9), is phosphorylated by kinases (see Example 7) and binds to PP2A/B γ (see Examples 3 and 6) and its activity/phosphorylation state is modulated by lithium, a compound art recognized to be useful for the treatment of bipolar disorder (see page 38, paragraph 2). As the Patent Office's reviewing courts have held, "[k]nowledge of the pharmacological activity of any compound is obviously beneficial to the public. It is inherently faster and easier to combat illnesses and alleviate symptoms when the medical profession is armed with an arsenal of chemicals having known pharmacological activities. Since it is crucial to provide researchers with an incentive to disclose pharmacological activities in as many compounds as possible, we conclude that adequate proof of any such activity constitutes a showing of practical utility." *Nelson v. Bowler*, 626 F.2d 853, 856, 206 U.S.P.Q. 881, 883 (C.C.P.A. 1980). Likewise, the Federal Circuit, in *Cross v. Iizuka*, 753 F.2d 1040, 1051, 224 U.S.P.Q. 739, 747-48 (Fed. Cir. 1985), stated:

We perceive no insurmountable difficulty, under appropriate circumstances, in finding that the first link in the screening chain, *in vitro* testing, may establish a practical utility for the compound in question. Successful *in vitro* testing will marshal resources and direct the expenditure of effort to further *in vivo* testing of the most potent compounds, thereby providing an immediate benefit to the public, analogous to the benefit provided by the showing of an *in vivo* utility.

Accordingly, reconsideration and withdrawal of the rejections under 35 U.S.C. §§ 101 and 112, first paragraph, is respectfully requested.

Claims 43-45 and 63-82 are provisionally rejected under the judicially created doctrine of “obviousness-type” double patenting over the claims of co-pending application Serial No. 10/744,796. Claims 43-45 and 63-82 are also provisionally rejected under 35 U.S.C. § 101 as claiming the same invention as that of claims 113-115 of the ‘796 application. Applicants respectfully submit that this rejection is moot as the ‘796 application is now abandoned. Accordingly, reconsideration and withdrawal of both provisional rejections is respectfully requested.

It should be understood that the amendments presented herein have been made solely to expedite prosecution of the subject application to completion and should not be construed as an indication of Applicants’ agreement with or acquiescence in the Examiner’s position. Applicants expressly reserve the right to pursue the invention(s) disclosed in the subject application, including any subject matter canceled or not pursued during prosecution of the subject application, in a related application.

In view of the foregoing remarks and amendments to the claims, Applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§ 1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

Applicants invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "Frank C. Eisenschenk". The signature is fluid and cursive, with the first name "Frank" being more prominent and the last name "Eisenschenk" written in a continuous script.

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Attachments: Form PTO/SB/08
Borsotto *et al.*, 2007